

ACUTE ISOLATED MYOCARDITIS IN NEWBORN INFANTS

BY

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Under such names as isolated myocarditis (Sellentin, 1904), Fiedler's myocarditis (Fiedler, 1899), and myocarditis perniciosa (Boikan, 1931), a rare myocardial disorder of unknown origin has been described which is characterized by progressive heart failure ending fatally after a course lasting weeks or months. In still rarer cases the duration of the illness is measured in days or hours. No age period is exempt from either form of the disease but the fulminating variety is perhaps commoner in young patients. Three cases occurring as early as the neonatal period have already been described. One was an infant aged 6 months (Singer, 1932), the others were newborn babies 9 and 5 days old respectively (Lind and Hultquist, 1949). To this small group the present report adds two other cases. Case 1, a boy, aged 4 weeks, was seen in October, 1950, and case 2, also a boy and aged 1 week, was seen a year later in October, 1951.

Because these young patients succumbed so quickly to the disease an unusually early type of myocardial lesion was preserved for examination. Particular interest therefore attaches to the histological findings in the cases described below.

Case Reports

Case 1. The patient was the sixth child of healthy parents. Two siblings died in infancy of bronchopneumonia following measles, the other three are healthy. There had been no illness in the household during the pregnancy and the child's life. The child was born in hospital and the delivery and puerperium were normal.

He remained perfectly well for four weeks and then developed a slight cough, became irritable and refused food. Twenty-four hours later he was admitted to hospital seriously ill. The face was slightly cyanosed, the respirations increased, the pulse was rapid but the temperature was normal. Lumbar puncture was done because of a bulging fontanelle but the cerebrospinal fluid was clear, not under pressure, and showed no increase in cells. Nothing further was found on general examination. Treatment with oxygen, penicillin and streptomycin produced no improvement and death occurred suddenly a few hours later. The antibiotic treatment comprised

two injections of penicillin each of 50,000 units and two of streptomycin each of 0.5 g.

Case 2. This child also happened to be the sixth member of his family. The parents are healthy and all the siblings alive and well. The pregnancy had been uneventful and the child was born at home after a normal labour. He fed well from the bottle and gave no sign of illness until the evening of the seventh day. The onset was then abrupt and the symptoms developed rapidly. The child seemed perfectly well when put into his cot after being fed at 10.30 p.m. but in a few minutes the mother noticed that the face and lips were bluish. When seen by the doctor shortly afterwards the child was pale and apathetic, and on admission to hospital he was in a seriously collapsed condition. The skin was cold and clammy, the respirations gasping. There was some blood and froth on the lips but no sign of injury in the mouth. Coramine was given by injection and the child was immediately removed to an oxygen tent and treated with penicillin and aureomycin. The clinical course was steadily downhill and the child died suddenly after an illness lasting only about 12 hours.

Penicillin was given in an initial dose of 100,000 units followed in six hours by another injection of 50,000 units. Aureomycin, 375 mg., was also given while the child was in hospital.

Necropsy Reports

The two cases were so alike that they may be described together. Both children were normally developed and showed no external evidence of disease, injury or congenital deformity. The lungs were oedematous and congested; a few petechial haemorrhages were scattered over the pleura and the cut surfaces. The hearts were similar in both cases; neither was enlarged or showed any pathological changes whatsoever when opened and dissected. There was nothing of note in the other organs.

Histology. Only the heart need be described. In the routine sections, cut through the anterior walls of the left atrium and ventricle and the anterior cusp of the mitral valve, there were multiple foci of muscle damage and cellular infiltration, which were very much alike in size and distribution in both

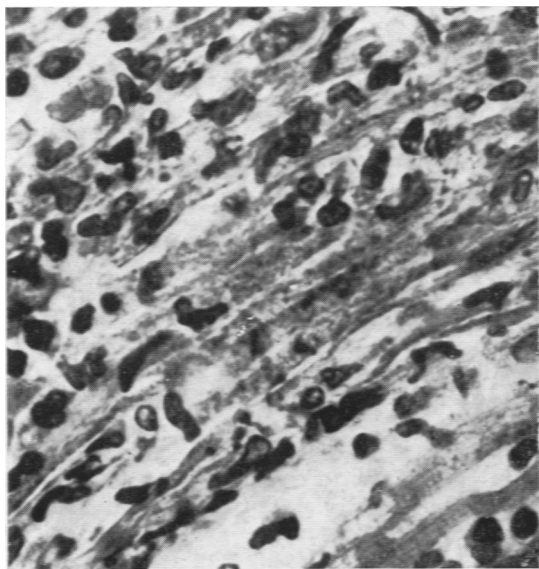


FIG. 1.—Earliest stage in the development of the lesion. Muscle striation is replaced by vividly eosinophilic hyaline granules and proliferation of muscle nuclei. (Kull's stain $\times 650$)

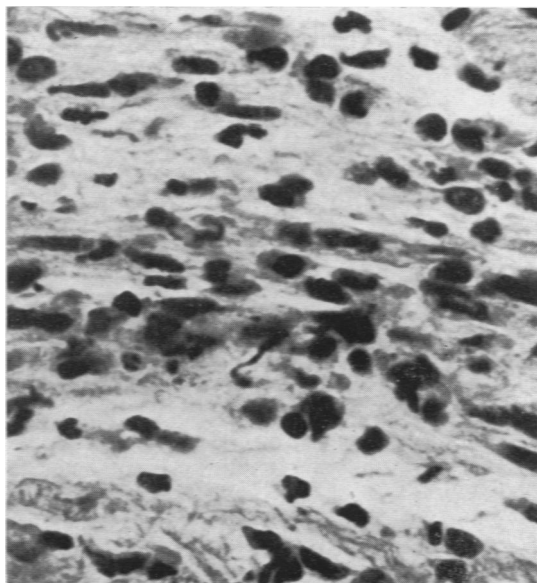


FIG. 2.—Later stage of the lesion showing myocardial degeneration, and muscle fibres filled with brownish-grey amorphous debris and degeneration of proliferated muscle nuclei. At the bottom may be seen longitudinal striations still visible in almost unaffected fibres. (Kull's stain $\times 650$)

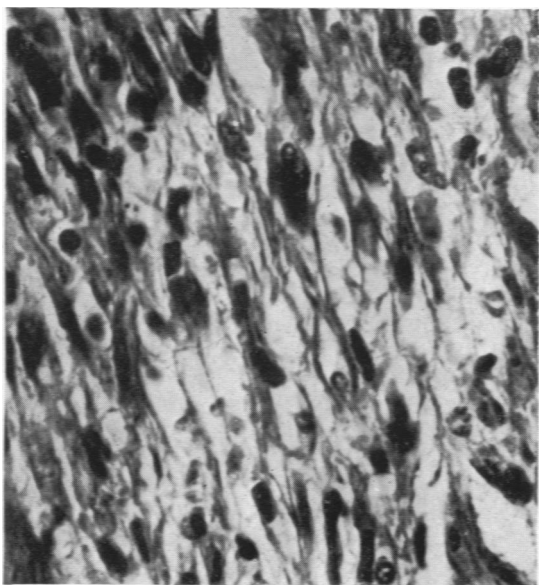


FIG. 3.—End stage of the lesion showing fenestrated appearance due to loss of sarcoplasm. (Kull's stain $\times 650$)

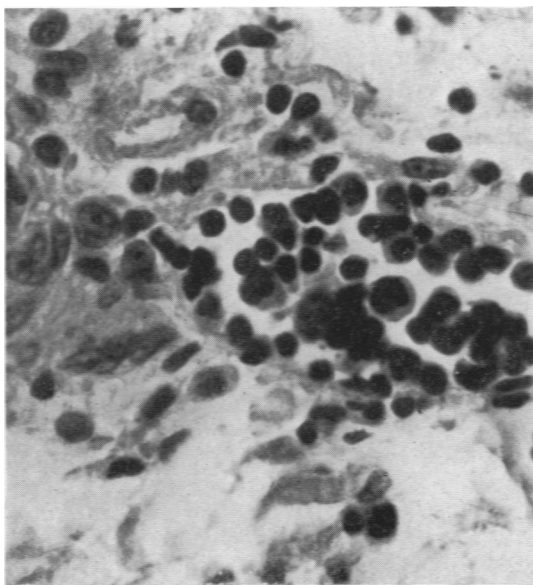


FIG. 4.—Perivascular lymphatic full of macrophages. (Kull's stain $\times 650$)

hearts. The largest occupied the whole strip of atrial wall in the section, the others, minute, were scattered throughout the ventricular myocardium. Differences in the cellular elements and in the fine detail of the muscle changes as seen in sections stained by a modified Kull's method (Millar, 1933) enabled the lesions to be arranged in a graded series.

In the most acute type of lesion (Fig. 1) the muscle fibres were swollen and crowded with large, intensely eosinophilic hyaline granules: no trace of normal striated sarcoplasm remained. The spaces between the fibres were occupied by proliferated muscle nuclei, but no adventitious cells were present. Lesions presumably of slightly longer standing (Fig. 2) showed progressive degeneration in the sarcoplasm and muscle nuclei, as well as infiltration by adventitious cells. The vividly red granules of altered sarcoplasm seen in the earlier lesions gave place to a brownish amorphous material; the muscle nuclei became shrunken, pyknotic or fragmented; mononuclears, eosinophils and lymphocytes began to appear between the fibres. The end of the process was seen in lesions from which sarcoplasm, muscle nuclei and all but a few inflammatory cells had disappeared, the loss of material giving a fenestrated appearance to the area (Fig. 3).

The epicardium, particularly in Case 1, was diffusely infiltrated by large mononuclears, eosinophils and lymphocytes and these cells also formed nodular collections in the adventitia of some of the arterioles. In the dilated lymphatics of the epicardium, again particularly in Case 1, clumps of large mononuclear cells, some containing ingested eosinophilic material, were often seen (Fig. 4).

Endocardial changes were limited to a slight proliferation of the lining cells wherever a myocardial lesion approached the surface. The valve cusps were not affected.

The essential pathological process was a degenerative change limited to the sarcoplasm of individual muscle fibres, the unaffected nuclei being free to proliferate, at least in the early stages. The degenerate sarcoplasm was rapidly removed by dissolution and phagocytosis, leaving empty spaces to mark the sites of the lesions. Inflammatory cells were absent from the lesions until the degenerative change was well advanced; thereafter mononuclears, eosinophils and lymphocytes appeared in succession. The character of the cellular infiltration and its relation to the muscle lesions showed that it was a secondary reactive phenomenon. The clinical circumstances and necropsy findings served to exclude all the usual causes of myocarditis and failed to reveal any primary disease in organs other than the heart. These cases therefore satisfy the criteria for

the diagnosis of isolated myocarditis (Saphir, Wile and Reingold, 1944).

Discussion

Cases of isolated myocarditis surviving for the usual time generally show conspicuous changes in the interstitial tissues of the heart. In a small minority the cardiac muscle is chiefly affected (Gouley, McMillan and Bellet, 1937; Biggart, 1950). The rare cases dying early in the disease are more evenly divided between interstitial and parenchymatous forms. Of the three such cases which have been reported in newborn infants one (Singer, 1932) showed myocardial degeneration, the others (Lind and Hultquist, 1949) interstitial changes only; two adult cases described by Lemke (1924) provided one example of each type of lesion, while that mentioned by Saphir *et al.* (1944) was of the interstitial type.

The classification of isolated myocarditis into a variety of histological types is best regarded at the present time as a descriptive convenience. There is nothing as yet to show that the histological differences correspond to separate disease processes. In fact, the cases described here provide suggestive evidence that some apparently unrelated histological changes may be linked together in the development of a single lesion. On the basis of the present findings the following conclusions seem therefore to be justified in these cases. The primary lesion was a rapidly resolving degeneration of unusual type in the cardiac muscle; it was associated with a cellular infiltration of the interstitial tissue which because of its slower tempo would probably persist after the muscle lesion subsided. Longer survival would therefore have meant a reversal of the histological picture from parenchymatous to interstitial myocarditis so that the cases might have been classified under either heading, depending on the time of death. According to this unifying hypothesis the pathogenesis of isolated myocarditis is seen as a succession of acute episodes of cardiac muscle injury associated with protracted interstitial reaction. Differences in the severity of the initial injury, variable secondary changes and death fortuitously at any stage of the disease would operate to produce the diverse histological appearances which have been described in different cases.

Summary

Two fatal cases of acute isolated myocarditis occurring in newborn infants are described.

The lesions in the myocardium were focal in distribution and showed a peculiar degenerative

change limited to the sarcoplasm of the affected muscle fibres.

The relationship of this parenchymatous lesion to the commoner interstitial type is discussed.

There was no response to treatment with various antibiotic agents.

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